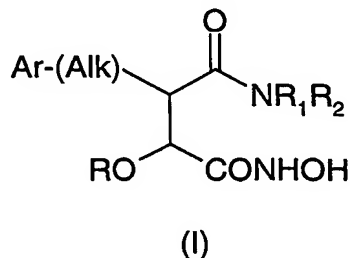


Claims:

1. A compound of formula (I), or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:

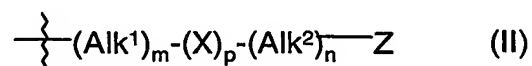
wherein

Ar represents an optionally substituted aryl, heteroaryl, C₃-C₈ cycloalkyl or heterocycloalkyl group;

R represents hydrogen or C₁-C₆ alkyl, or C₃-C₆ cycloalkyl;

Alk represents a divalent C₁-C₅ alkylene or C₂-C₅ alkenylene radical; and

R₁ and R₂ taken together with the nitrogen atom to which they are attached form a first heterocycloalkyl ring which is optionally fused to a second C₃-C₈ cycloalkyl or heterocycloalkyl ring, the said first and second rings being optionally substituted by at least one group of formula (II):

wherein

m, p and n are independently 0 or 1;

Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms;

Alk¹ and Alk² independently represent optionally substituted divalent C₁-C₃ alkylene radicals;

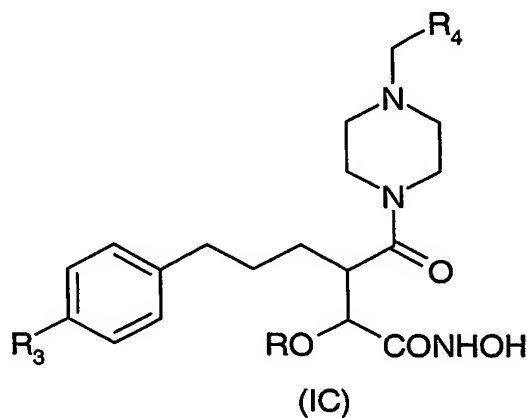
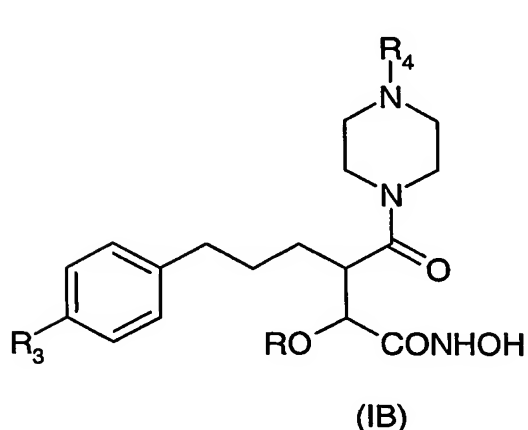
X represents -O-, -S-, -S(O)-, -S(O₂)-, -C(=O)-, -NH-, -NR₃-,
-S(O₂)NH-, -S(O₂)NR₃-, -NHS(O₂)-, or -NR₃S(O₂)-, where R₃ is C₁-C₃ alkyl.

2. A compound as claimed in claim 1 wherein R is hydrogen.
3. A compound as claimed in claim 1 wherein R is methyl.
4. A compound as claimed in claim 1 wherein R is ethyl, n-propyl, isopropyl, n-, sec- or tert-butyl, cyclopropyl, or cyclopentyl.
5. A compound as claimed in any of the preceding claims wherein Ar is a 5- or 6- membered monocyclic aryl or heteroaryl ring, which is optionally substituted by at least one substituent selected from (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), -COOH, -COOR^A, -COR^A, -SO₂R^A, -CONH₂, -SO₂NH₂, -CONHR^A, -SO₂NHR^A, -CONR^AR^B, -SO₂NR^AR^B, -NH₂, -NHR^A, -NR^AR^B, -OCONH₂, -OCONHR^A, -OCONR^AR^B, -NHCOR^A, -NHCOOR^A, -NR^BCOOR^A, -NHSO₂OR^A, -NR^BSO₂OR^A, -NHCONH₂, -NR^ACONH₂, -NHCONHR^B, -NR^ACONHR^B, -NHCONR^AR^B, or -NR^ACONR^AR^B wherein R^A and R^B are independently C₁-C₃ alkyl, phenyl or a 5- or 6-membered monocyclic aryl or heteroaryl ring.
6. A compound as claimed in claim 5 wherein an optional substituent is in the 4- position in the case of a 6-membered ring, or in the 2- and/or 3- position in the case of a 5-membered ring.
7. A compound as claimed in any of the preceding claims wherein Ar is optionally substituted phenyl, 2-, 3-, or 4-pyridyl, 2-, or 3-thienyl, or 2-, or 3-furanyl.
8. A compound as claimed in any of the preceding claims wherein optional substituents in Ar are selected from methoxy, ethoxy,

trifluoromethoxy, methyl, ethyl, trifluoromethyl, hydroxyl, mercapto, fluoro, chloro, and bromo.

9. A compound as claimed in claim 5 wherein Ar is 4-(C₁C₃alkoxy)phenyl.
10. A compound as claimed in claim 5 wherein Ar is 4-ethoxyphenyl
11. A compound as claimed in any of the preceding claims wherein Alk is -CH₂-, -CH₂CH₂-, -CH₂CH(CH₃)-, -CH₂CH₂CH₂-, -CH₂CH₂CH₂CH₂-, -CH=CH-, -CH₂CH=CH-, -CH₂CH=CHCH₂-, or -CH=CHCH=CH-.
12. A compound as claimed in any of the preceding claims wherein -NR₁R₂ forms a pyrrolidiny, morpholy, or thiomorpholy ring
13. A compound as claimed in any of claims 1 to 11 wherein -NR₁R₂ forms a piperidiny, or piperaziny ring
14. A compound as claimed in any of the preceding claims wherein in the group (II), when present, p is 0, Z is hydrogen and at least one of n and m is 1.
15. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, m, n and p are all 0 and Z is a carbocyclic or heterocyclic ring directly linked to a ring carbon or ring nitrogen of the -NR₁R₂ group.
16. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, p is 0, at least one of m and n is 1, and Z is a carbocyclic or heterocyclic ring linked to a ring carbon or ring nitrogen of the -NR₁R₂ group via a C₁-C₆ alkylene linker between Z and the -NR₁R₂ ring.
17. A compound as claimed in any of claims 1 to 13 wherein in the group (II), when present, p is 1.

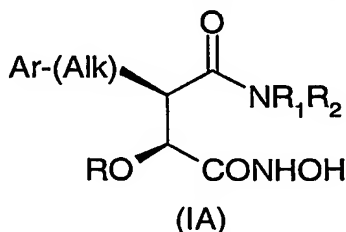
18. A compound as claimed in claim 1 of formula (IB) or (IC) or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



wherein R is hydrogen or methoxy, R₃ is trifluoromethyl, trifluoromethoxy C₁-C₃alkoxy, hydroxy, or halo; R₄ is (i) -SO₂R₅ or -COR₅ wherein R₅ is C₁-C₆alkyl or phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, optionally substituted by (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy or (ii) phenyl or monocyclic heteroaryl having 5 or 6 ring atoms; optionally substituted by (C₁-C₃)alkyl, (C₁-C₃)alkoxy, hydroxy, hydroxy(C₁-C₃)alkyl, mercapto, mercapto(C₁-C₃)alkyl, (C₁-C₃)alkylthio, halo, trifluoromethyl, trifluoromethoxy.

19. A compound as claimed in claim 18 wherein a heteroaryl ring forming part of R₄ is pyridyl, pyrimidinyl, triazinyl, thienyl, or furanyl.

20. A compound as claimed in any of the preceding claims having the stereochemical configuration shown in formula (IA):



21. A compound as claimed in claim 1, which is selected from the group consisting of:

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide.

3R-(6,7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2RS-methyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2,6-RS-dimethyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(thiomorpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-piperidine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzo[1,3]dioxol-5-ylmethyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-ylmethyl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-benzylpiperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyrimidin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethyl-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-chloro-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(4,6-dimethoxy-[1,3,5]triazin-2-yl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(acetyl-methyl-amino)-piperidine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(methyl-propyl-amino)-piperidine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-benzyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-isobutyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-phenyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-3RS-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(3S,4-dibenzyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-3RS-phenyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-2S,N-dihydroxy-4-oxo-3R-(4-trifluoromethoxy-benzyl)-butyramide.

3R-benzyl-2S,N-dihydroxy-4-morpholin-4-yl-4-oxo-butylamide.

3R-(4-Benzyloxy-benzyl)-2S,N-dihydroxy-4-oxo-4-piperidin-1-yl-butylamide.

2S,N-dihydroxy-3R-(4-hydroxy-benzyl)-4-oxo-4-piperidin-1-yl-butylamide.

4-(4-benzo[1,3]dioxol-5-ylmethyl-piperazin-1-yl)-3R-(4-benzyloxy-benzyl)-2S,N-dihydroxy-4-oxo-butylamide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-piperidine-1-carbonyl)-6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-3R-(6,7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide

3R-(2S-benzyl-4-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(toluene-4-sulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(5-bromo-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-[4-(5-benzenesulfonyl-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-[4-(4-butoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-2,3,6-trimethyl-benzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

3R-[4-(3,4-dimethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-methoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

6-(4-methoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

6-(4-fluoro-phenyl)-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-2S-hydroxy-hexanoic acid hydroxyamide.

6-(4-fluoro-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester,

6-(4-ethoxy-phenyl)-2S-methoxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide.

22. A pharmaceutical composition comprising a compound as claimed in any of the preceding claims, together with a pharmaceutically acceptable carrier.

23. A compound as claimed in any of claims 1 to 21 for use as a medicament.

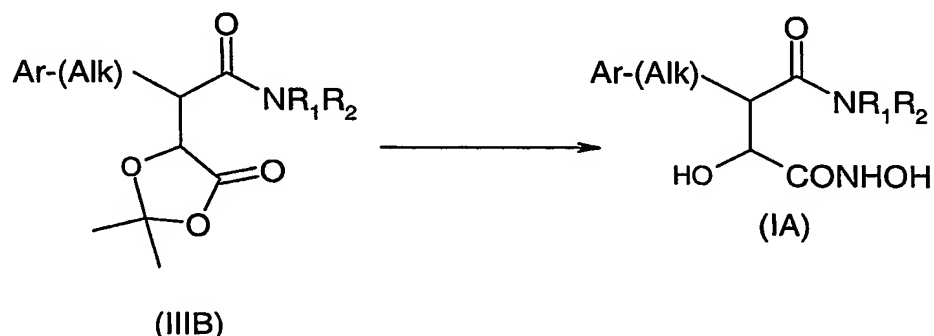
24. A method of treatment or prophylaxis of diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9 in mammals, which method comprises administering to the mammal an effective amount of a compound as claimed in any of claims 1 to 21

25. The use of a compound as claimed in any of claims 1 to 21 in the preparation of an agent for the treatment or prophylaxis of diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9.

26. A method as claimed in claim 24 or a use as claimed in claim 25 wherein the disease or condition is bone resorption, tumour growth or invasion by secondary metastases; rheumatoid arthritis, septic arthritis, osteoarthritis, periodontitis, gingivitis, corneal ulceration, cardiac hypertrophy, acute respiratory distress syndrome, neuroinflammatory disorders, e.g. multiple sclerosis; restenosis; emphysema; fibrotic disease e.g. fibrosis post radiotherapy, kerotid scarring, liver fibrosis and cystic fibrosis; chronic obstructive pulmonary disease; bronchitis; asthma; autoimmune disease; transplant rejection (e.g. graft versus host disease); cystic fibrosis; psoriasis; psoriatic arthritis; degenerative cartilage loss; inflammatory gastric conditions, e.g. Crohn's disease, inflammatory bowel disease, and ulcerative colitis; atopic dermatitis, epidermolysis bullosa; epidermic ulceration; a neuropathy or nephropathy e.g. interstitial nephritis, glomerulonephritis or renal failure; ocular inflammation; liver cirrhosis, Sjogren's syndrome; or an inflammatory condition of the nervous system.

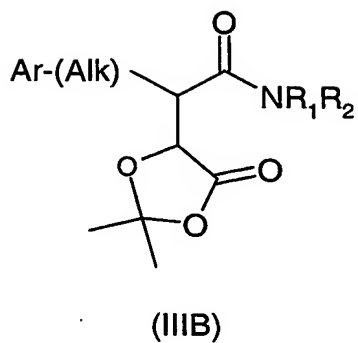
27. A method as claimed in claim 24 or a use as claimed in claim 25 wherein the disease or condition is fibrotic disease, multiple sclerosis, emphysema, bronchitis or asthma.

28. A method of preparing metalloproteinase inhibitors of formula (IA) according to any of claims 1 to 21 wherein R is hydrogen, comprising the de-protection and/or transformation step of:



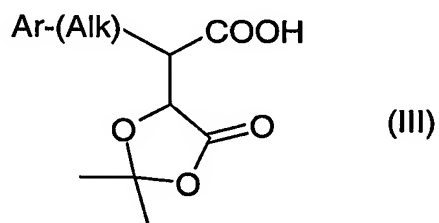
wherein Ar, Alk, R₁ and R₂ are as defined in any of claims 1 to 16.

29. A compound of formula (IIIB)



wherein Ar, Alk, R₁ and R₂ are as defined in any of claims 1 to 19.

30. A process for the preparation of a compound as claimed in claim 29 comprising comprising the step of reacting a compound of formula (III)



with a cyclic amine HNR₁R₂, wherein Ar, Alk, R₁ and R₂ are as defined in any of claims 1 to 19.